

RESEARCH ARTICLE

# Antiplasmodial activity of New Caledonia and Vanuatu traditional medicines

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## Abstract

**Context:** With the emergence of strains multiresistant to antimalarial drugs, the search for new active molecules remains a priority. Ethnopharmacology appears to be a good method of selection in such investigations. **Objective:** The aim of this research work is to select plants used in Melanesian traditional medicine, in New Caledonia and Vanuatu, which should be a promising source for the isolation of new antimalarial drugs.

**Materials and methods:** Forty-seven plant extracts belonging to 12 families, traditionally used by the Melanesian people or belonging to an antimalarial known genus, were screened *in vitro* for antimalarial activity on *Plasmodium falciparum* chloroquine (CQ)-resistant (FcB1) and CQ-sensitive (HB3) strains. They were also tested for their inhibitory effects on a protein kinase (Pfnek) and their cytotoxicity on human breast adenocarcinoma (MCF7) cells.

**Results:** Among all extracts, four displayed strong *in vitro* activities against *P. falciparum*: *Gardenia urvillei* Montrouzier, *Scleria polycarpa* Boeckeler, *Terminalia catappa* L. and *Acrornychia laevis* J.R. & J.G. Forster, the latter being also toxic on MCF7 cells. Except for the extracts of *S. polycarpa*, all others that were active on *P. falciparum*, also possess an inhibitory effect on Pfnek.

**Discussion and conclusion:** These results confirm that ethnopharmacology is an excellent approach for such investigations. The two countries considered clearly present advantages in the field. Indeed, local populations keep their traditional knowledge alive, and their flora is exceptionally rich. In New Caledonia, the high endemicity rate (74%) ranks the island as one of the world's biodiversity hotspots. As a consequence, chances to discover new active natural compounds are also high.

**Keywords:** *Acrornychia laevis*, *Gardenia urvillei*, medicinal plants, Melanesia, MCF7 cells, Pfnek, *Plasmodium falciparum*, *Scleria polycarpa*, *Terminalia catappa*

## Introduction

New Caledonia is a French overseas territory in the South Pacific, about 2000 km east of Australia. The Republic of Vanuatu is an archipelago of 80 uninhabited islands, about 500 km NNE of New Caledonia. These two countries have a tropical climate characterized by a rainy season with an average temperature of 30°C from November to April and a dry season from

May to October. According to WHO (2005), malaria is present in 105 countries and territories, 10 of which are situated in the West Pacific, including Vanuatu. People living in countries with endemic malaria generally treat themselves with traditional remedies or use them as an alternative or complementary treatment (Wilcox & Bodeker, 2004). Since only a few plants from the South Pacific area have been investigated for antiplasmodial

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activity (Verotta et al., 2001; Hay et al., 2004), we decided to search for novel natural bioactive antiparasmodial compounds within the flora of this region. New Caledonia and Vanuatu appear to be interesting lands for two reasons: on the one hand, local populations keep their traditional knowledge alive, on the other, the flora is exceptionally rich with a 74% endemism rate in New Caledonia (Jaffre et al., 2001). Thus, the island is considered as one of the world's hotspots of biodiversity. Consequently, chances to discover new active natural molecules are very likely.

Plant selection was based on ethnopharmacological data collected amongst local traditional healers. For biological evaluations we chose species which are traditionally used to treat fevers (the main symptom of malaria) and/or stomach troubles (a symptom frequently associated with malaria). Plant extracts were prepared and tested against *Plasmodium falciparum* *in vitro* culture. We also tested their capacity to inhibit Pfnek, a specific *P. falciparum* protein kinase involved in the completion of the parasite cycle (Reininger et al., 2005).

The pfnek-1 assay was chosen for two main reasons: firstly, there are no *Plasmodium* cultures in New Caledonia because of legal restrictions; secondly, because a direct link has been observed, in previous studies, between both antiparasmodial and Pfnek-1 activities (Lebouvier et al., 2009).

## Materials and methods

### Plant material

During a 15-year-long program on natural substances, carried out in Vanuatu and New-Caledonia, 17 native or endemic plants belonging to 12 families from New Caledonia and Vanuatu were selected on the basis of ethnopharmacological studies and bibliographical research. Species with strong medicinal indications generally used for fever treatment and gastro-intestinal disorders were selected (Table 1). Plants were collected in 2004 and herbarium voucher specimens were deposited at the Noumea IRD Herbarium (NOU). These latter were used by IRD botanists in order to identify species.

Selected plant parts (Table 2) were sampled, oven-dried at 40°C for 48 h and ground before being immediately extracted by maceration. In the case of *Terminalia catappa*, leaves were also extracted fresh.

### Preparation of plant extracts

All chemicals come from Sigma Aldrich (Saint-Quentin Fallavier, France). Dried powdered materials (60 g) were extracted by shaking maceration in 250 mL of ethanol (80%) or dichloromethane for 3 h at room temperature. The macerate was then dried and again extracted with methanol under the same conditions. The extracts were filtered and dried under reduced pressure.

### Protein kinase inhibition test (Pfnek)

Antiparasmodial activity of extracts was first estimated with a protein kinase assay. Recombinant Pfnek-1 was purified from a transformed ampicillin-resistant bacteria *Escherichia coli* (BL21 strain) which produces a fusion protein carrying a glutathioneS-transferase fragment on one terminal end and the catalytic domain of Pfnek-1 on the other. The glutathioneS-transferase activity is used for enzyme purification by affinity chromatography on a glutathione resin (Dorin et al., 2001). The protein kinase activity was estimated by measuring  $^{33}\text{P}$  incorporation into  $\beta$ -casein, using  $\gamma$ -[ $^{33}\text{P}$ ]-ATP (Perkin Elmer, Courtaboeuf, France) as a phosphate donor. Test compounds were dissolved in DMSO and incubated in 20 mM Trizma pH 7.5, containing 20 mM  $\text{MgCl}_2$ , 10 mM NaF and 10  $\mu\text{M}$  ATP.  $\beta$ -Casein (3 mg/mL) and  $\gamma$ -[ $^{33}\text{P}$ ]-ATP were introduced before the addition of 1  $\mu\text{g}$  GST-Pfnek-1, which started the kinase reaction. 5  $\mu\text{Ci}$  of  $\gamma$ -[ $^{33}\text{P}$ ]-ATP were used per reaction. After incubation at 30°C for 30 min, each solution was transferred to a phosphocellulose filter paper (chromatography paper P81; Whatman-cation exchanger). After four successive washes with 1%  $\text{H}_3\text{PO}_4$ , the acid-precipitable radioactivity was measured using a liquid scintillation analyzer Packard 1600TR. The  $\text{IC}_{50}$ , defined as the concentration of compounds inhibiting 50% of the enzyme activity, was estimated from the dose-response curves. Roscovitine (Sigma) was used as positive control.

### *In vitro* assays on *P. falciparum*

Antiparasmodial activities were determined *in vitro* against the chloroquine-resistant (FCB1) and CQ-sensitive (HB3) strains of *P. falciparum*. *P. falciparum* was cultivated according to Trager and Jensen (1976), on glucose-enriched RPMI 1640 medium supplemented with 10% human serum at 37°C. The original microdilution technique of Desjardins et al. (1979) was then modified as described in Valentin et al. (1997). *Plasmodium* infected erythrocytes were plated at 3% parasitemia (5% hematocrit) with [ $^3\text{H}$ ]-hypoxanthine (Amersham, London) (0.8  $\mu\text{Ci}$ ), in 96-well microtiter plates, and exposed to different concentrations of the crude extracts. Plates were incubated for 48 h, at 37°C in a 5%  $\text{CO}_2$  atmosphere. Microtiter plates were then frozen-defrosted and each well was harvested onto a glass fiber filter. At this point the incorporated [ $^3\text{H}$ ]-hypoxanthine was determined with a beta-counter (Perkin Elmer, Courtaboeuf, France). Controls were performed to assess the background (negative control) and the parasite growth (positive control). Growth curves (inhibition versus extract concentration) were plotted and the  $\text{IC}_{50}$  was determined graphically. Chloroquine was used as the inhibitor standard.

Results were classified according to Rasoanaivo et al. (2004): If the  $\text{IC}_{50}$  is less than 0.1  $\mu\text{g/mL}$ , the activity was considered very good; from 0.1 to 5  $\mu\text{g/mL}$ , good; from 5 to 10  $\mu\text{g/mL}$ , moderate; over 11  $\mu\text{g/mL}$  the extract was considered inactive.

Table 1. Studied plants and their Melanesian traditional uses.

Plant species: family, status, localization	Voucher specimen (n)°	Vernacular name [Melanesian language village, or NCF (New Caledonian French)]	Part(s) used and preparation	Traditional use in medicine: treatment or target	Literature, notes and references
<i>Acronychia laevis</i> J.R. Forster & G. Forster (Rutaceae), native, New Caledonia	AD11, JWHL 81	<i>gerit</i> (jawe, BasCoulna); <i>hmelexeci</i> (drehu, Lifou)	Scraped bark lixiviated	Fever, influenza	Antimalarial use in Palawan Island traditional medicine, Philippines (Horgen et al., 2001) Unpublished data (Bourret)
<i>Alyxia stellata</i> (J.R. & G. Forster) Roemer & Schultes (Apocynaceae) native, New Caledonia	ML 11	<i>hnyim</i> (drehu, Lifou), <i>nyènyög</i> (iai, Ouvea), <i>waninitha</i> (nengone, Mare)	Juice of masticated bud, decoction of scraped bark, orally	Internal aches and influenza	Chronic diarrhea and fevers (Planchon, 1894) Unpublished data (Hnawia; Bourret)
<i>Calophyllum caledonicum</i> Vieillard (Clusiaceae) endemic, New Caledonia	JWRG 22	<i>pio</i> , <i>pi y o</i> (nemi, Bas Coulna, Ouayaguet), <i>mí</i> (ajie, houailou)	Scraped lixiviated bark and wood	Tonic, gum edema, all kinds of hemoptysis	Purgative and emetic gum, diuretic bark (Rageau, 1973); antimalarial xanthonones (Hay et al., 2004) Unpublished data (Bourret; Waikedre)
<i>Citrus macroptera</i> Montrouzier (Rutaceae) native, New Caledonia, Vanuatu	JW 78	<i>oranger sauvage</i> , <i>oranger ancien</i> (NCF)	Leaves	Diarrhea, rheumatism	(Cabalion et al., 2005)
<i>Codiaeum peltatum</i> (Labillardière) P.S. Green (Euphorbiaceae) native, New Caledonia	JWRG 23	<i>croton</i> (NCF), <i>ceulo</i> (jawe, Ouayaguet)	Macerated leaves, orally	Influenza, tuberculosis	Unpublished data (Waikedre)
<i>Crossostylis grandiflora</i> Brongniart & Gris (Rhizophoraceae) endemic, New Caledonia	LIT 0326	<i>palétuvier de montagne</i> (NCF) <i>doaren</i> (nemi, Tendo) <i>dùren</i> (nemi, Bas Coulna)	Stems Bark lixiviated decoction of leaves, local application	Constipation Cleaning wounds	Astringent, perhaps antipyretic barks (Rageau, 1973) Unpublished data (Bourret)
<i>Crossostylis multiflora</i> Brongniart & Gris (Rhizophoraceae) endemic, New Caledonia	JWRG 20	<i>hêtre nouveaux</i> , <i>chêne gris de Farino</i> (NCF) <i>opwärö</i> (paici, Tchamba)	Leaves Bark lixiviated	Ulcerations	Astringent, perhaps antipyretic barks (Rageau, 1973) Unpublished data (Bourret)
<i>Garcinia puat</i> Guillaumin (Clusiaceae) endemic, New Caledonia	JWRG21	<i>taaveu</i> (xârâcùù, Thio); <i>fôn</i> (xârâcùù, Canala); <i>faux houp</i> (NCF)	Gum Edible fruit	Purgative, drastic and hydragogue	Antimalarial xanthonones and <i>Garcinia spp.</i> (Grosvenor et al., 1995; Hay et al., 2004; Horgen et al., 2001; Likhitwitayawuid et al., 1998a, b; Tona et al., 1999; 2004) (Rageau, 1973) unpublished data (Bourret; Cabalion)
<i>Gardenia urvillei</i> Montrouzier (Rubiaceae) endemic, New Caledonia	JW 77	<i>tiaré des forêts sèches</i> (NCF) <i>uru</i> (ajie, Houailou), <i>ug</i> (drehu, Lifou), <i>hök</i> (iai, Ouvea)	Leaves	No traditional medicinal use	Antiplasmodial triterpens; other species used as in antimalarial remedies in Sudan (El-Tahir et al., 1999; Suksamrarn et al., 2003) Unpublished data (Bourret)
<i>Glochidion billardieri</i> Baillon (Euphorbiaceae) endemic, New Caledonia	AD10, JWHL82	<i>hmana</i> (iai, Ouvea)	Leaves and bark buds masticated	Antipyretic, shoulder or kidney pains, headaches, infected injuries, all “diseases”	Unpublished data (Waikedre)
<i>Homalium deplanchei</i> (Vieillard) Warburg (Flacourtiaceae) endemic, New Caledonia	LIT 0781	<i>cascade d'or</i> (“golden waterfall”), <i>didrem</i> (drehu, Lifou)	Leaves, decoction, orally	Tonic	Unpublished data (Bourret)

Table 1. continued on next page

Table 1. Continued.

Plant species: family, status, localization	Voucher specimen (n) <sup>o</sup>	Vernacular name (Melanesian language village, or NCF [New Caledonian French])	Part(s) used and preparation	Traditional use in medicine: treatment or target	Literature, notes and references
<i>Manikara dissecta</i> var. <i>pancheri</i> (Baillon) Maas (Sapotaceae), endemic var., New Caledonia; native sp., Vanuatu	LIT 0537	<i>buni</i> , <i>bugny</i> (ncf) <i>pö</i> (drehu, Lifou), <i>fenök</i> (iai, Ouvea), <i>angai</i> (nengone, Mare)	Juice of expression of leaves, orally	Against "all diseases"	a Kenyan species traditionally used against malaria, <i>M. butugi</i> (Munguti, 1994) Unpublished data (Bourret)
<i>Meryta</i> sp. (Araliaceae) endemic, New Caledonia	TRO 629		Bark	Antipyretic	Unpublished converging data, concerning <i>Meryta coriacea</i> antipyretic (Bourret)
<i>Murraya crenulata</i> Olivier (Rutaceae) native, New Caledonia, Vanuatu	ML 10	<i>puifelö</i> (drehu, Lifou), <i>ibon</i> (nengone, Mare), <i>nigöt</i> (iai, Ouvea)			Antimalarials in a <i>Murraya</i> sp. (Likhitwitayawuid et al., 1999) unpublished data (Bourret; Hnawia; Waikedre)
<i>Persicaria subsessilis</i> (R. Brown) K.L. Wilson. Syn: <i>Polygonum subsessile</i> R. Brown (Polygonaceae) native, New Caledonia, Vanuatu	JWRG13	<i>pharuyak</i> (nixumwak, Koumac region) <i>chöuu</i> (xârâcùù & xârâgurè, Thio)	Leaves Leaves macerated	Women's diseases Prevention and treatment of children's diseases e.g. candidiasis	(Cabalion et al., 2005) Unpublished data (Cabalion; Hnawia; Waikedre)
<i>Scleria polycarpa</i> Boeckeler. Syn: <i>Scleria scorbiculata sensu</i> Christophersen 1935 (Cyperaceae) native, New Caledonia, Vanuatu	JWRG25	<i>noyoteptep</i> (motlav, Vanuatu)  <i>malo</i> (nemi, Ouayaguet)	Maceration of fresh flowers, oral way Aerial parts contused and macerated, local application	Hoarseness  Internal pains in legs	(Vienne, 1981-1982)  Unpublished data (Waikedre)
<i>Terminalia catappa</i> L. (Combretaceae) introduced, New Caledonia, Vanuatu	DN 94	<i>badamier</i> (NCF); <i>betelèm</i> (ajie, Houailou); <i>macatre</i> (drehu, Lifou); <i>maketr</i> (iai, Ouvea); <i>keëda</i> (jawe, Oubatche and yuanga, Bonde); <i>kiida</i> (nêlêmwa and nixumwak and nelâyü, Poum and Koumac and Balade); <i>salite</i> and <i>saltis</i> (mota, Vanuatu); <i>natles</i> (mota lava, Vanuatu); <i>natapoa</i> (bislama, Vanuatu)		Various uses: antipyretic, antimalarial, astringent, sudorific, antidiarrhetic, antirheumatic uses	nêlêma and nixumwak names (Bril, 2000); nelâyü name (Ozanne-Riviere, 1988); mota and mota lava names (Vienne, 1981-1982); other names unpublished data (Bourret; Cabalion; Hnawia; Waikedre)

### Cytotoxicity assay

Human breast adenocarcinoma (MCF7) cells were grown in DMEM culture media containing 2 mM L-glutamine (Bio Witter) supplemented with 5% fetal calf serum (FCS) (Sigma Aldrich, Saint-Quentin Fallavier, France) and incubated under standard conditions (37°C, 5% CO<sub>2</sub>). All experiments were carried out using cells in the exponential growth phase. Cells were trypsinized, suspended in DMEM containing 5% FCS and seeded (40,000 cells/well) in 96-well plates. After 24 h, the medium was replaced by a fresh one containing various dilutions of the extract. Fresh complete medium without drugs was used as positive control. At the end of the treatment, cell viability was evaluated by measuring the mitochondrial enzyme succinate dehydrogenase activity. This test used sodium 3,3-(1-phenyl-amino-

carboxyl)-3-4-tetrazolium + bis-(4-methoxy-6-nitro)] benzene sulfonic acid hydrate] (XTT) as substrate which was converted to a formazan product detected spectrophotometrically at 450 nm (Jullian et al., 2005).

Doxorubicin was used as the control drug.

### Results and discussion

Forty-seven extracts from 17 plants, belonging to 12 families were screened for antiplasmodial activity against *Plasmodium falciparum* infected erythrocytes and for Pfnek inhibition. Traditional uses are listed in Table 1 and antiplasmodial activities are listed in Table 2. Only four extracts, *Acronychia laevis* J.R. & J.G. Forster (Rutaceae), *Gardenia urvillei* Montrouzier

(Rubiaceae), *Scleria polycarpa* Boeckeler (Cyperaceae) and *Terminalia catappa* L. (Combretaceae), revealed to be active against all *P. falciparum* strains resistant or sensitive to chloroquine, with an  $IC_{50} < 10 \mu\text{g/mL}$ . Chloroquine used as control showed an  $IC_{50}$  of 120 nM against FCB1 and 36 nM against HB3 strains.

Nineteen extracts showed an inhibitory activity above 50% on Pfnek at a concentration of 25  $\mu\text{g/mL}$  while roscovitine has an  $IC_{50}$  of 20  $\mu\text{M}$  (7  $\mu\text{g/mL}$ ). Three extracts inhibited both *P. falciparum* *in vitro* growth and Pfnek, i.e., *Gardenia urvillei*, *Terminalia catappa* and *Acronychia laevis*. Only *Acronychia laevis* proved to be cytotoxic in

Table 2. Activity of plant extracts on HB3 and FCB1 *Plasmodium falciparum* strains, Pfnek and MC7 cells.

Species	Part of plant	Extract type	Pfnek (% inhibition)	HB3 ( $IC_{50}$ $\mu\text{g/mL}$ )	FCB1 ( $IC_{50}$ $\mu\text{g/mL}$ )	MCF7 ( $IC_{50}$ $\mu\text{g/mL}$ )
<i>Acronychia laevis</i>	Leaves	$\text{CH}_2\text{Cl}_2$	<b>52.7</b>	> 20	> 20	
	Leaves	MeOH	<b>60.8</b>	> 20	> 20	
	Bark	$\text{CH}_2\text{Cl}_2$	<b>50.7</b>	<b>10</b>	<b>5</b>	<b>3</b>
	Bark	MeOH	49.0	> 20	20	
<i>Alyxia stellata</i>	Entire plant	$\text{CH}_2\text{Cl}_2$	<b>69.5</b>	20	> 20	
	Leaves	$\text{CH}_2\text{Cl}_2$	19.3	20	20	
	Stems	$\text{CH}_2\text{Cl}_2$	46.6	20	20	
	Entire plant	MeOH	44.1	20	> 20	
<i>Calophyllum caledonicum</i>	Leaves	$\text{CH}_2\text{Cl}_2$	0.7	15	> 20	70
	Leaves	EtOH	38.8	20	> 20	
	Bark	$\text{CH}_2\text{Cl}_2$	9.1	17	> 20	> 100
	bark	EtOH	13.3	> 20	> 20	
<i>Citrus macroptera</i>	Leaves	$\text{CH}_2\text{Cl}_2$	42.5	> 20	> 20	
	Leaves	EtOH	41.5	> 20	> 20	
<i>Codiaeum peltatum</i>	Leaves	EtOH	26.5	10	> 20	
	Bark	EtOH	44.9	> 20	> 20	
<i>Crossostylis grandiflora</i>	Leaves	$\text{CH}_2\text{Cl}_2$	47.0	16	> 20	
	Leaves	MeOH	<b>54.1</b>	20	> 20	
	Bark	$\text{CH}_2\text{Cl}_2$	47.7	17	> 20	
	Bark	MeOH	<b>60.7</b>	20	> 20	
<i>Crossostylis multiflora</i>	Leaves	$\text{CH}_2\text{Cl}_2$	5.4	> 20	> 20	
	Bark	EtOH	13.4	> 20	> 20	
<i>Garcinia puat</i>	Bark	EtOH	40.2	10	> 20	
<i>Gardenia urvillei</i>	Leaves	EtOH	<b>54.7</b>	<b>5</b>	<b>5</b>	<b>100</b>
	Bark	EtOH	<b>62.9</b>	10	> 20	> 100
<i>Glochidion billardieri</i>	Leaves	$\text{CH}_2\text{Cl}_2$	43.4	> 20	> 20	
	Leaves	MeOH	<b>54.8</b>	20	20	
	Bark	$\text{CH}_2\text{Cl}_2$	18.2	20	> 20	
	Bark	MeOH	<b>73.4</b>	20	> 20	
<i>Homalium deplanchei</i>	Leaves	$\text{CH}_2\text{Cl}_2$	<b>64.3</b>	20	> 20	
	Leaves	MeOH	<b>65.4</b>	20	20	
	Bark	$\text{CH}_2\text{Cl}_2$	NT	10	> 20	
	Bark	MeOH	48.6	17	> 20	
<i>Manikara dissecta</i> var. <i>pancheri</i>	Leaves	$\text{CH}_2\text{Cl}_2$	<b>63.4</b>	> 20	> 20	
	Leaves	MeOH	<b>60.8</b>	> 20	> 20	
	Bark	$\text{CH}_2\text{Cl}_2$	47.2	> 20	> 20	
	Bark	MeOH	<b>54.8</b>	> 20	> 20	
<i>Meryta</i> sp.	Bark	$\text{CH}_2\text{Cl}_2$	<b>61.6</b>	10	> 20	> 100
	Bark	MeOH	NT	> 20	> 20	
<i>Murraya crenulata</i>	Leaves	EtOH	<b>59.8</b>	> 20	20	
	Leaves	$\text{CH}_2\text{Cl}_2$	<b>67.9</b>	> 20	> 20	
<i>Polygonum subsessile</i>	Leaves	$\text{CH}_2\text{Cl}_2$	3.6	> 20	> 20	
	Stems	$\text{CH}_2\text{Cl}_2$	7.1	> 20	> 20	
<i>Scleria polycarpa</i>	Leaves	$\text{CH}_2\text{Cl}_2$	2.5	<b>5</b>	<b>5</b>	> <b>100</b>
<i>Terminalia catappa</i>	Dried leaves	$\text{CH}_2\text{Cl}_2$	11.9	> 20	> 20	
	Fresh leaves	EtOH	<b>68.0</b>	<b>10</b>	<b>7.7</b>	> <b>100</b>

Remarkable activities are in bold type in the table



the MCF7 model at 3 µg/mL while doxorubicin had an  $IC_{50}$  of 4 µM (2.3 µg/mL).

#### ***Acronychia laevis* J.R. et J.G. Forster (Rutaceae)**

Common in New Caledonia, *Acronychia laevis* is rarely used in traditional medicine as an antipyretic. Its vernacular name is “hmelexeci” in Drehu language (Lifou Island). According to Horgen et al. (2001), species of *Acronychia* genus were considered as antiparasitodials. The extract of *A. laevis* stems inhibited Pfnek at 50.7% and had an  $IC_{50}$  of 5 µg/mL against FcB1 strain of *P. falciparum*, but the same extract was strongly cytotoxic against MCF7 cells at 3 µg/mL. The presence of quinoline and acridone alkaloids has been isolated from *Acronychia* species (Cui et al., 1999; Michael, 2001). Such compounds could explain the observed antimalarial and cytotoxic activities of *A. laevis*.

#### ***Gardenia urvillei* Montrouzier (Rubiaceae)**

*Gardenia urvillei* is endemic to New Caledonia, commonly named “tiaré des forêts sèches” (dry forests “tiaré”). This plant is not considered as an antipyretic in traditional medicine in New Caledonia, but according to the literature the genus *Gardenia* contains some triterpenes with antiparasitodial activities, their  $IC_{50}$  ranging from 1.5 to 2.9 µg/mL (El-Tahir et al., 1999; Suksamrarn et al., 2003). Ethanol extract of *G. urvillei* leaves inhibited the protein kinase (54.7%) and was active against *P. falciparum* ( $IC_{50}$  = 5 µg/mL) without toxicity on MCF7 cells at concentrations up to 100 µg/mL.

#### ***Scleria polycarpa* Boeckeler (Cyperaceae)**

Sometimes misnamed *Scleria scrobiculata* auct. plur., non Nees & Meyen in old publications, *Scleria polycarpa* can be found from Samoa and Tonga to Melanesia, northeast Australia, Marianas and Carolinas to West Malaysia (Smith, 1979). Its vernacular name is “noyoteptep” in Motalava, Vanuatu, where the maceration of fresh flowers was used to treat hoarseness (Vienne, 1981–1982). Macerations of leaves were also recommended against fevers, diarrhea and gastro-intestinal problems in Indonesia (Grosvenor et al., 1995). It also exists in Fiji where it is known by its local name, but Fijians do not use it in their traditional medicine (Smith, 1979). The dichloromethane extract of dried leaves had no activity on the protein kinase (2.5% inhibition) but it showed an  $IC_{50}$  of 5 µg/mL against FcB1 strain of *P. falciparum* and was not cytotoxic against MCF7. A study on the medicinal plants used to treat malaria in Madagascar (Rasoanaivo et al., 1992) revealed that *Scleria griegifolia* Riedley leaves were used in decoctions in rural areas to treat fevers. This interesting activity observed with *S. polycarpa* may indicate the occurrence of potential antiparasitodial compounds in the genus *Scleria*. Moreover, the non-volatile compounds in the genus *Scleria* remain unknown. *S. polycarpa* is definitely a good candidate for further phytochemical investigations.

#### ***Terminalia catappa* L. (Combretaceae)**

*T. catappa* is an introduced species in New Caledonia and Vanuatu, commonly named “badamier”. People use this plant as an antipyretic, astringent, sudorific and antidiarrhetic (Rageau, 1973). According to Cambie and Ash (1994) a decoction of leaves or stems is also used against fevers and other symptoms in the South Pacific islands. Also, in Taiwan fallen leaves are used as an herb to treat liver diseases (Lin & Kan, 1990). In Suriname, a tea made from the leaves is prescribed against dysentery and diarrhea (DeFilipps et al., 2004). It is also thought that the leaves contain antioxidant (Lin et al., 2001) and agents for prevention of cancers (although they have no demonstrated anticarcinogenic properties) (Morioka et al., 2005) as well as chromosome breakage, and sickle cell anemia antileukogenic characteristics (Mgbemene & Ohiri, 1999).

We showed that an ethanol extract of fresh leaves inhibited 60% of the protein kinase and 50% of *P. falciparum* growth at 7.7 µg/mL, without cytotoxicity against MCF7 cells at 100 µg/mL. *T. catappa* is known to contain high amounts of hydrolysable tannins (Lin et al., 2001). They could explain the antiparasitodial activity; indeed hydrolysable tannins isolated from *Combretum molle* (R. Br. Ex. G. Don.) Engl. & Diels showed a weak antiparasitodial activity (Asres et al., 2001).

### **Conclusion**

This study brings important insights to malaria research as the field is in constant need for alternative anti-malarial drugs. It appears to be the first attempt to screen antiparasitodial activities in plant extracts issued from New Caledonian flora. It concerned 17 medicinal species traditionally used for fever and gastro-intestinal disorder treatments, in New Caledonia or Vanuatu. Some of them showed both *in vitro* activities against *Plasmodium falciparum* and Pfnek and no cytotoxicity against MCF7 cells. Four were revealed to be very interesting, with important activities. Unfortunately, one of them, *Acronychia laevis*, was active but also cytotoxic. In contrast, three other plants of our sample, *Gardenia urvillei*, *Scleria polycarpa* and *Terminalia catappa* provide a foundation for further exploration of a new effective herbal drug and allow the isolation, and identification of antimalarial active compounds.

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## Declaration of interest

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